

**Brian J. Cummings, Ph.D.**

*Professor  
Physical Medicine, Neurological Surgery,  
Anatomy & Neurobiology*

*Sue & Bill Gross Stem Cell Research Center  
845 Health Science Road  
Room 226  
Irvine, CA 92697-1705  
Office: (949) 824-3254  
Fax: (949) 824-9728*

**July 17, 2019, Additional List of Letters of Support for Cummings Application (TRAN1-11548)**

- 1. Brian J. Cummings, PhD**, Professor, Department of Physical Medicine, Neurological Surgery, Anatomy & Neurobiology
- 2. Don C. Reed**, Vice President of Public Policy for Americans for Cures Foundation, Palo Alto, CA
- 3. Michael Chopp, PhD**, Scientific Director, Neuroscience Institute, Oakland University, Rochester, MI
- 4. Phillip J. Horner, PhD**, Director, Center for Neuroregeneration, Houston Methodist, Houston TX
- 5. Leslie M. Thompson, PhD**, Professor & Chancellor's Fellow, Depart. of Neurobiology and Behavior, UC Irvine
- 6. Victor Perez, MSW**, Rehabilitation Institute of Southern CA, Orange County, CA
- 7. Susan Connors**, President & CEO. Brain Injury Association of America, Vienna, VA
- 8. Mohammed Ahmed, MD**. Medical Director, Kaizen Brain Center, San Diego, CA



Brian J Cummings, Ph.D.

Professor & Vice-Chair for Research

PHYSICAL MEDICINE AND REHABILITATION/NEUROLOGICAL SURGERY

ANATOMY & NEUROBIOLOGY

SUE & BILL GROSS STEM CELL CENTER

PHYSICAL MEDICINE & REHAB/NEUROSURGERY

2026 Gross Hall

845 Health Sciences Road

UC Irvine, Irvine, CA 92697-1750

Tel: (949) 824-3254 Fax: 824-9728

[cummings@uci.edu](mailto:cummings@uci.edu)

July 20, 2019

Maria Bonneville ([mbonneville@cirm.ca.gov](mailto:mbonneville@cirm.ca.gov))

Vice President of Administration

Executive Director of the ICOC

### TRAN1 - An optimized human neural stem cell line for the treatment of traumatic brain injury.

**Incidence.** TBIs are a silent epidemic.

- TBIs are the leading cause of death and disability worldwide, affecting more people than brain, breast, colon, lung, and prostate cancer **combined**.
- Nearly 2 million Americans (230,000 Californians) experience a TBI leading to hospitalization yearly.
- 40% of patients discharged after a TBI have long-term disabilities, at an estimated cost to society of \$76 billion (~\$9 billion to California) each year.
- 25% of combat casualties are TBI related.

**Unmet Need.** TBI can lead to concentration and memory problems, personality changes, and anxiety, aggression, or risk-taking behavior.

- There are no approved therapies for TBI, whether pharmacological or stem cell based.
- The medical need from TBI is on par with Alzheimer's disease, as TBI affects younger people who will live longer with a disability.
- TBI increases the risk of developing Alzheimer's disease (AD); a treatment for TBI could ultimately reduce the number of people with AD, or enable new AD treatments.

**Our Program.** We propose to complete GMP manufacture and pre-clinical testing of a stem cell therapy for TBI. We believe a cell therapy is a good strategy for promoting recovery of cognitive/emotional function because of the potential for long-term biological action (vs transient pharmacokinetics) and the multi-target effects of human neural stem cells (hNSCs).

- We are the **only** CIRM-funded program addressing traumatic brain injury.
- We have shown efficacy in **FOUR** separate experiments using hNSC manufactured 3 times
- We have **improved learning & memory** and **reduced anxiety-like behaviors** in TBI models.
- We can **extend** the treatment window to 30 days post-injury using **frozen** aliquots of hNSCs

**We have evidence for multiple mechanisms of action (MOAs), including:**

- Making new neurons and glia (support cells)
- Helping the injured brain to make its **own** new neurons
- Protecting the brain from ongoing degeneration
- Reducing inflammation

CIRM funding will enable long-term animal safety tests, inclusion of female rats, an expanded transplant window and a large animal model with imaging parallel human imaging.

### Summary of Grants Working Group reviews and brief response

The CIRM Grants Working Group of scientific experts has recommended our TBI program for funding four times. We have only been awarded funds twice (not including this TRAN1).

- We were initially funded by an early translation award (ETAIL) in 2011; using this funding, we successfully developed an animal model of TBI and screened two research-grade cell populations.
- We were recommended for funding of a Discovery award in 2016, however, CIRM was short of funds and we were skipped over. These data were reviewed by a Department of Defense scientific panel & recommended for funding, but denied administratively to avoid funding embryonic research.
- We resubmitted to CIRM for a Discovery award in 2017 and were again recommended for funding in June of 2017. With that funding, we compared multiple embryonic and fetal cell lines and ultimately showed that clinical-grade Shef6 human neural stem cells worked as well as research-grade Shef6 cells. These clinical grade Shef6 NSCs are the focus of this TRAN1 award.

Below, we address the three concerns reviewers raised during the GWG discussion.

**1. Rodent models of TBI are too focal, and may not translate to humans.** We attach a letter from Michael Chopp, one of the foremost experts in preclinical TBI research, with over 250 relevant publications, who is also conducting clinical trials for TBI. He argues that while the model we use is “focal”, the model results in diffuse injury and widespread inflammation as well. Indeed, we observe diffuse injury in this “focal” model. Also, our TRAN1 includes expanding our efficacy studies to non-human primates with Dr. Daadi, the Director of the Southwest National Primate Research Center.

**2. The long period of cell manufacture could lead to changes in the cells over time or genetic instability.** Since the submission of this grant, we have tested (A) combining CD133 and CD34 cell sorting and (B) using FAC cell sorting rather than MAC cell sorting to increase yield. These two approaches combined have enabled us to shorten manufacture time by more than 25%. Further, in addition to the GMP manufacture expertise of AIVITA, we have enlisted Dr. Jeanne Loring, who has been studying the genomics and epigenetics of human pluripotent cells for more than 15 years, to guide us on cell stability. Dr. Loring will oversee RNAseq analysis on 3 parallel manufacturing runs to monitor for mutations of concern and to create a molecular phenotype that can be used to compare runs. We will also use Single Nucleotide Polymorphism (SNP) analysis to detect copy number variations and any loss of heterozygosity in our cells.

**3. Because obtaining an INTERACT meeting appears unlikely based on the advanced stage of our program, a reviewer recommended refraining from initiating the large animal study and moving up the pre-IND meeting to enable earlier FDA feedback on study design.** This is sound advice, and if funded, we will work with CIRM staff to modify the timeline to make such an approach feasible.

**In Sum:** We are very appreciative of the GWG Tier 1 score and to CIRM for their recommendation to fund our TRAN1-11548 application. As in the past, the reviews were overwhelmingly positive. We hope that the ICOC will support further funding of our work. If successful, we will be able to address a severe unmet need. Use of standard medical and neurosurgical procedures and practices for the delivery of Shef6.133.hNSCs would enable widespread use of this therapy and could also impact other neurodegenerative disorders.

**Lastly,** we would like to add that our work over these past 8 years has been supported by 10 CIRM Bridges interns, 3 of whom will continue work on TBI should this TRAN1 be funded. An additional CIRM Bridges intern, who worked on the hNSC cell derivation protocols, was hired several years ago by AIVITA and will be working on this TRAN1 from AIVITA's side in GMP manufacture. Without these interns, this work could not have been completed.

Thank you for considering funding for our proposed program.

Sincerely,



Brian J Cummings, PhD

and



Aileen J Anderson, PhD

July 11, 2019

## SUPPORT FOR TRAUMATIC BRAIN INJURY PROJECT TRAN1

Public Comment by Don C. Reed

Will there be a Prop 71 part 2? That decision is not mine to make. But I absolutely know what I do want, and that is a major renewal of funding.

The best way to move toward that goal, I believe, is to take on a truly huge problem—and they just don't get any bigger than Traumatic Brain Injury, TBI.

Every year, more than 200,000 Californians receive a traumatic brain injury, at a financial cost of roughly \$9.6 billion, an amount more than three times California's entire ten year investment in CIRM. Across our country, 1.7 million citizens suffer a TBI—at the staggering expense of \$76.5 billion.

More people have a traumatic brain injury than are affected by cancers of the brain, breast, colon, lung and prostate -- put together.

What is it like to have a traumatic brain injury? Often compared to Alzheimer's disease, TBI destroys memory, and brings emotional confusion to the sufferer. While TBI affects similar numbers of Californians with Alzheimer's, TBI is much less known, and might be called a silent epidemic.

The Primary Investigator for this project, Brian Cummings, told me of a family summer camp for children to which he brought his daughter. While there, he met a woman who had been a soldier in the Iraq war, where she twice received TBIs from one of those ghastly home-made bombs, the Improvised Explosive Device, an IED. What brought the meaning of the Traumatic Brain Injury home to Dr. Cummings was that this woman soldier—could not remember which child were her children.

Traumatic Brain Injury, at present, is incurable.

As you know, for more than 25 years I have been supporting research for the related condition of spinal cord injury. And four of our greatest research champions are: Aileen Anderson, Hans Keirstead, and Gabriel Nistor and Brian Cummings. All four of these outstanding SCI scientists— this time led by Brian Cummings as the TBI expert-- will be involved in this project.

Their goal? "Transplantation of human neural stem cells could lead to improvements in learning, memory and emotion (to) significantly change a patient's quality of life, (with) considerable economic impact to California". In addition, four young scientists from CIRM's Bridges program will bring the energy and passion of youth to this endeavor.

This is CIRM at its very best. I urge your support.

**Don C. Reed**

<http://www.stemcellbattles.net> (sign up for my free newsletter!)

*Don Reed is author of the new book, "CALIFORNIA CURES! How the California Stem Cell Program is Fighting Your Incurable Disease!" available now at <http://bit.ly/californiacures>. For a 20% discount, use code "WSPY2PP20"!*

*Reed is also Vice President of Public Policy for Americans for Cures Foundation; opinions voiced here as an individual may or may not reflect those of the Foundation.*

VISIT <http://www.AmericansforCures.org>



## HENRY FORD HOSPITAL

The Department of Neurology  
2799 West Grand Boulevard  
Detroit, MI 48202 USA

Michael Chopp, PhD, FAHA, FESO  
Vice Chairman, Department of Neurology  
Scientific Director, Neuroscience Institute  
Zolton J. Kovacs Chair in Neuroscience Research  
Distinguished Professor, Physics, Oakland University, Rochester, MI  
Henry Ford Health System  
Neurology Research, Education & Research Building, Room 3056  
(313) 916-3936 Office  
(313) 916-1318 Fax  
[mchopp1@hfhs.org](mailto:mchopp1@hfhs.org)

July 16, 2019

Dear CIRM Independent Citizens Oversight Committee (ICOC),

I am Vice Chairman of Neurology Research and the Scientific Director of the Neuroscience Institute at Henry Ford Hospital in Detroit Michigan. For more than 30 years, my lab has focused on the pathophysiology of stroke and traumatic brain injury; mechanisms of neuroprotection, and cell-based or pharmacological neurorestorative therapies for stroke, traumatic brain injury, and neurodegenerative disease. I have authored more than 750 peer reviewed publications and have been awarded more than \$80 million in total funding; our lab currently has 15 active NIH grants.

HFH is one of the leading research centers in the world in translational neuroscience and restorative neurology and my lab was the first lab to use cell-based therapies such as human umbilical cord blood cells and mesenchymal stem cells (MSCs) as well as exosomes derived from MSCs to try to develop treatments for stroke, TBI, and neurodegenerative diseases. These restorative therapies have promising potential for the treatment of neural injury. In fact, I have recently formed a partnership with NeuroTrauma Sciences, LLC (NTS), a biopharmaceutical company, to develop and test exosomes for the treatment of stroke and TBI.

I have been following Drs Brian Cummings' and Aileen Anderson's progress on the preclinical and clinical testing of human neural stem cells for spinal cord injury, and more recently traumatic brain injury. I have also had the opportunity to visit them at UC Irvine several years ago and observe their thoughtful and deliberative approach to cell-based therapies for neurotrauma.

Dr. Cummings' recent publications on Shf6 derived hNSCs provide strong evidence for the therapeutic potential of these cells for TBI. Of particular relevance is the potential of these cells to modulate neuroinflammation and promote host neurogenesis – even at sites distant from the initial transplantation. In my expert opinion, these characteristics negate any concerns about the particular animal model used (as CCI is the standard in the field) and the focal damage to hippocampus. While CCI is “focal”, there is no question that CCI also results in diffuse injury and inflammation as well (as shown in both my work and that of Dr Cummings).

I strongly encourage CIRM to continue funding such potentially transformative work – particularly coming from such a strong California based team with a proven track-record in bringing neural stem cell therapies to clinical trial. Indeed, if this TRAN1 grant is successful, I can imagine Shf6 hNSCs being used for other indications as well.

Sincerely,

A handwritten signature in black ink, appearing to read "MChopp", written over the printed name and title.

Michael Chopp, PhD  
Vice Chairman, Division Research  
The Department of Neurology  
Scientific Director, Neuroscience Institute  
Henry Ford Hospital / Henry Ford Health System



July 17, 2019

Dear Members of the Independent Citizen's Oversight Committee,

I trained with Dr. Fred Gage and became a staff scientist at the Salk Institute in 1998. In 2001, I joined the Department of Neurological Surgery at the University of Washington in Seattle, where I was a member of the Institute for Stem Cell and Regenerative Medicine. In 2015, I was recruited to the Houston Methodist Research Institute as the Scientific Director of the Center for Neuroregenerative Medicine and the Co-Director of the Center for Regenerative and Restorative Neurosurgery.

The Center for Neuroregeneration strives to discover therapies for people who suffer from disorders to the Central Nervous System. As Director, I oversee the research programs of 12 faculty across a broad spectrum of basic, preclinical, and clinical efforts and have experience with the regulatory hurdles of translational research. The Center is comprised of laboratories with expertise in neural stem cell biology, neural activity and stimulation, robotics, cell growth, myelin and the genetic regulation of plasticity.

My research focuses on the role of glial and neural progenitor cells in the regeneration of the injured nervous system. I have authored >150 neuroscience publications. During normal aging and following trauma or disease, brain and spinal cord stem cells fail to replace needed circuitry. We are developing approaches to modify the fate of neural stem cells to increase cellular repair after spinal cord and brain injury. Neural regeneration strategies are also being applied to stroke, glaucoma and motor/cognitive decline associated with aging.

I am well versed in the research programs of Drs. Anderson and Cummings, as I was a Christopher Reeve Foundation fellow with Dr. Anderson from 1998-2002 and have visited their labs at UC Irvine multiple times. As part of Methodist's training program, we invite noted experts for a monthly seminar series. This June, both Dr. Cummings and Dr. Anderson each gave 1-hour presentations on their current CIRM funded work. The 100+ neuroscientists in attendance saw the pre-clinical work that comprise their CIRM application on a neural stem cell therapy for TBI. They were very impressed with the totality of the preclinical package in support of moving Sh6 human neural stem cells forward to a clinical trial. I also had the opportunity to discuss their work in greater detail, and I am confident that they have carefully considered the issues surrounding cell manufacture, safety testing, adding a large animal model, and the regulatory environment.

I strongly support their application and hope the CIRM Board votes to approve this promising program. TBI is a significant unmet medical need and the state of California is well situated to address this problem and win future public support by tackling a condition that effects so many of its citizens. From my perspective, a cell therapy for TBI, supported from inception to preclinical development to clinical trial by CIRM, is precisely what the neuroscience research community had hoped CIRM would be able to accomplish in its initial funding period.

Yours sincerely,



**Philip J. Horner, PhD**  
Director, Center for Neuroregeneration, Houston Methodist



LESLIE M. THOMPSON, PH.D.  
CHANCELLOR'S PROFESSOR

Psychiatry and Human Behavior  
Neurobiology and Behavior  
4060 Gross Hall  
845 Health Sciences Road  
Irvine, CA 92697-1705

July 19, 2019

## Letter of Support for TRAN1-11628

Dear CIRM ICOC,

I am writing this letter with my strong support for the TRAN1 application of Cummings, Anderson and Keirstead to use hESC-derived neural stem cells for the treatment of TBI.

I am a Chancellor's Professor at the University of California Irvine and member of the Sue and Bill Gross Stem Cell Center. For 30 years, my lab has focused on understanding the underlying mechanisms and development of therapeutic strategies for Huntington's disease (HD), culminating recently in a CIRM funded CLIN1 application to use human ES-derived neural stem cells stem transplantation as a treatment for this devastating disease. Over the years, I have had the great opportunity to work as a close colleague with Drs. Cummings and Anderson as our groups have developed stem cell-based approaches for traumatic brain injury (TBI) and HD, respectively. We have shared data and strategies and mutually planned preclinical studies, FDA interactions, evaluated the highest standards for quality control and reproducibility of the cell lines we are using to develop for clinical trials. I can unequivocally say that Drs. Cummings and Anderson are scientists who approach stem cell biology and translation for human disease with the highest scientific rigor possible. The proposed studies are assuredly of the highest standards and will be transformative for individuals with TBI. This disorder has an urgent need with a staggeringly high number of individuals affected - 2.5 million American's a year alone. I have witnessed the devastation of this disease on families who have no options for treating their loved ones.

The proposed studies by this strong group is based on years of experience, research and clinical application of stem cell-based treatments for spinal cord injury (SCI) together with Dr. Keirstead. They now bring that expertise to a potential treatment for TBI, with an extremely strong pre-clinical dataset, publications and replication of the Shef6 effect on TBI models and evidence of efficacy with a 30-day delay and freeze-thaw cell product that can be immediately applied to the clinic. A further significant strength is the expertise and support of Dr. Keirstead and Aivita who will provide scientific, manufacturing, quality systems and regulatory expertise to the program and have a history of clinical trials and commercialization application for treatments of human disease using stem cell-based approaches. Finally, AIVITA has a former CIRM Bridges intern now working with the team who has prior experience with the Shef6 cells, which provides additional expertise for transfer of cell manufacturing to an external company in the future.

This is a remarkable team that has demonstrated success in the translation of stem cell biology to human disease by bringing neural stem cell therapies to clinical trial, who will tackle an urgent human need and ultimately will likely produce a high return on investment for CIRM and taxpayers.

I urge the board to consider funding this important grant.

Sincerely,

A handwritten signature in cursive script that reads "Leslie M. Thompson".

Leslie M. Thompson, Ph.D.



**REHABILITATION INSTITUTE OF SOUTHERN CALIFORNIA  
COMMUNITY BASED ADULT SERVICES PROGRAM**

**130 Laguna Rd.  
Fullerton, CA 92835  
(714) 680-6060**

July 18, 2019

California Institute for Regenerative Medicine  
Independent Citizens Oversight Committee  
1999 Harrison Street, Suite 1650  
Oakland, CA 94612

**Re: Support for the Study of human neural stem cells to treat brain injuries**

My name is Victor Perez and I am a Master of Social Work with the Rehabilitation Institute of Southern California (RIO) assigned to the city of Fullerton site, which is one of three California sites, including locations in the cities of Orange and San Clemente. At RIO, we have been supporting California residents who have suffered a traumatic brain injury (TBI) since 1950. I have worked with RIO for over two-years, counseling patients and their families. Most of our TBI patients are considered high-acuity and require significant assistance with activities of daily living (ADLs) and 24-hour supervision. Our average length of stay is 8.8 years. Although recently, we had to discharge a patient to a higher level of care facility due to early onset dementia, possibly linked to his TBI. Additionally, RIO hosts an active TBI support group.

There are currently no treatments for the long-term effects of TBI. Approximately 230,000 California's suffer a TBI each year. While not all of those injured will suffer permanent effects, the toll on patients and their families, and the economic cost to California is staggering. If we presume that every Californian who suffers a TBI this year has a partner and two parents, this means nearly 1 million California residents are impacted each year. We also know that the economic costs to the state are roughly 9.6 billion dollars per year.

People with moderate to severe TBI typically face a variety of chronic health problems. These issues add costs and burden to people with TBI, their families, and society. Among those still alive 5 years after injury:

- 57% are moderately or severely disabled
- 55% do not have a job (but were employed at the time of their injury)
- 50% return to a hospital at least once.
- 33% rely on others for help with everyday activities

TBI survivors often experience complications of aphasia and loss of independence. Unfortunately, I often witness this struggle... of observing what I can only relate to the phenomenon of lethologica or the "tip of the tongue" experience. Can you imagine forgetting how to speak or losing your independence with very little resources available? I can. I can also tell you that TBIs are emotional and that patients and families suffer from anxiety, anger, frustration, confusion, and depression.

Picture Brian, a 15-year-old young man, as he is experiencing the livelihood of being that teenager learning how to skateboard, not knowing his life would forever be altered because of a car accident that would change the way his brain functions. Having known what it was like to live a fairly independent life, he now must learn how to relive not being able to dictate to his body what he wants it to do, nor to speak and be understood. These deficits gradually led to the frustration of a new lifestyle he did not ask for. Eventually, Brian would grow to lose interest in daily activities and develop depression. Fortunately, Brian has two loving parents who have advocated for him to be enrolled in a RIO program where he can have his needs met, including addressing the emotional distress related to his TBI. If a cell therapy could even partially improve Brian's abilities, his life would be greatly improved.



Greg, a 42-year-old male was commuting home when he was in a car accident. Greg would forever lose his ability to ambulate freely, speak his mind, and most importantly, raise his daughter. Greg experienced emotional distress and anger stemming from his TBI. Having been frustrated with his life-altering situation, Greg worked tenaciously towards an independent life. Unfortunately, this led him to become increasingly angry with his situation as he faced the severity of his situation. Now Greg relies heavily on medication to work through his anger. Unfortunately, Greg has a difficult time with effectively applying what he learns in counseling for anger management, because of his TBI-related memory impairments. Greg now must learn to not only live a life of increased dependence but watch his daughter be raised by his mother. A cell therapy that improved his memory or reduced his anger/anxiety could significantly impact Greg's life and the life of his family.

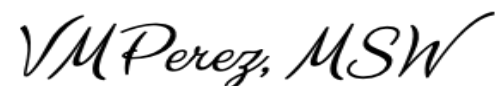
Brian and Greg are examples of the many individuals who have been referred to RIO for services that would support their needs as survivors of a TBI. Unfortunately, even at RIO, we are limited to how many individuals we can serve because of limited occupancy space, counselors, and resources.

There is a desperate need to accelerate stem cell treatments for people who suffer from TBIs. People with TBIs deserve to have awareness and access to treatments that can prove to be most effective than the tools that exist today. Without successful intervention, moderate and severe TBIs can lead to a lifetime of physical, cognitive, emotional, and behavioral changes. These changes often affect a person's ability to function in their everyday life. Despite initial hospitalization and inpatient rehabilitation services, about 50% of people with TBI will experience a further decline in their daily lives or die within 5 years of their injury.

On behalf of the Rehabilitation Institute of Southern California, my colleagues and patients have sent me here to enthusiastically endorse Dr. Cummings' project based at UC Irvine, which aims to establish safety and efficacy of human neural stem cells as a therapy for TBI. This work could lead to a clinical trial in just a few years. While Dr. Cummings' team needs CIRM funding to support completion of his preclinical work; equally important, Californians and their families impacted by TBI need the hope that a well-designed, state supported cellular therapy will soon be available. We all hope that stem cell-based therapies targeting neuroregeneration will be able to translate into the clinic shortly.

If successful, Dr. Cummings' work could also impact not only those with a TBI, but also those with spinal cord injuries, Parkinson's disease, and even Alzheimer's disease. As a social worker on the front lines of this battle, I look forward to the day when I can refer clients to cellular TBI clinical trials instead of just referring them to brain banks to support research toward new and better TBI treatment options.

Thank you for your time.

A handwritten signature in black ink that reads "VM Perez, MSW". The signature is written in a cursive, flowing style.

---

Victor M. Perez, MSW  
Medical Social Worker

July 18, 2019

California Institute for Regenerative Medicine  
Independent Citizens Oversight Committee  
1999 Harrison Street, Suite 1650  
Oakland, CA 94612

Re: **Support for the Study of hNSCs to treat TBI**

Dear CIRM Independent Citizens Oversight Committee (ICOC),

Imagine not knowing the difference between a hairbrush, a toothbrush, and a paint brush or forgetting which goes on first: your shoes or your socks. This is what life can be like for the 2.5 million children and adults in the United States who sustain a traumatic brain injury (TBI) each year. According to the Centers for Disease Control and Prevention (CDC), 5.3 million people live with a TBI-related disability at a cost to our nation exceeding \$82 billion annually.

The Brain Injury Association of America (BIAA) is the nation's oldest and largest brain injury patient advocacy organization. On behalf of BIAA, our members and our nationwide network of state brain injury organizations and local support groups, I write to urge your support for Dr. Cummings grant application to study the use of hNSCs to treat TBI.

Finding a cure for TBI is critical to the nation and to the people of California. Millions of Californians work in the construction industry and are at risk for sustaining a brain injury from a fall. Data from the Bureau of Labor Statistics indicates that falls are a leading cause of death for construction employees, accounting for a third of fatalities recorded in 2017. Interestingly, falls are the leading cause of TBI (40.5%). Californians are also very active in outdoor activities, increasing the risk of injury. The majority of falls result in mild traumatic brain injuries, also known as concussion. People who sustain these so-called mTBIs often do not receive treatment, leaving them vulnerable to feeling anxious, depressed, and sometimes suicidal. This is especially true for athletes and America's servicemen and women who survive multiple mTBIs. Dr. Cummings is a recognized expert in both acute TBIs and repeat mild TBIs/concussions.

All of us at BIAA strongly believe in maximizing basic, clinical, preventive and TBI health services research and funding. Californians and all Americans desperately need to support this effort in bringing neural stem cell therapies to clinical trial. We need to find a cure for TBI! If this TRAN1 grant is successful, I can imagine Shef6 hNSCs being used for other indications as well.

Sincerely



Susan H. Connors  
President/CEO



**KAIZEN**  
BRAIN CENTER  
Your Mind, Your Future.

Dear CIRM Independent Citizens Oversight Committee (ICOC)

I am a Neuropsychiatrist, board certified by the American Board of Psychiatry and Neurology. In addition, I'm currently Medical Director of Kaizen Brain Center, located in La Jolla, an associate physician and academic instructor at the University of California San Diego (UCSD), and an affiliate staff member at Hoag Memorial Hospital, located in Newport Beach, in the Department of Neurology & Psychiatry there. As you can surmise, my patients represent Southern California.

As a specialist in both Memory Disorders/Dementia and Brain Injury Medicine, I have expertise in both fields to treat people suffering from memory and cognitive disorders due to various neurodegenerative disorders, such as Alzheimer's Disease, Fronto Temporal Dementia, Lewy Body Dementia, and Traumatic Brain Injury/Concussion, Chronic Traumatic Encephalopathy (CTE), and I have been uniquely trained from a neurology, psychiatry, and rehab perspective in treating veterans with TBI and former NFL players.

We are now learning that the consequences of concussion, and particularly repeated or multiple concussions such as those sustained by athletes in a wide range of sports have their own sequelae of repercussions, leading to increased risk of developing chronic traumatic encephalopathy (CTE). Deficits are associated with thinning of the white matter and loss of cortical neurons. Californians and all Americans desperately need to support this effort in bringing neural stem cell therapies to clinical trial. Indeed, if this TRAN1 grant is successful, I can imagine Shaf6 hNSCs being used for other indications as well.

Sincerely,

Mohammed Ahmed, MD  
Neuropsychiatrist  
Memory & Cognitive Disorders  
Brain Injury Medicine

CALL 866.277.2659 FAX 858.779.2511

ADDRESS 4180 La Jolla Village Drive, Suite 240, La Jolla, CA 92037

[KAIZENBRAINCENTER.COM](http://KAIZENBRAINCENTER.COM)