Mind MATTERS

SANDERS-BROWN PUBLICATION ON AGING | Fall 2022

Sanders-Brown Center on Aging

PROGRESS THROUGH PARTICIPATION

It is my pleasure to welcome you to the 2022 issue of Mind Matters, the Sanders-Brown Center on Aging magazine. Within these pages you will find features highlighting our groundbreaking work in the study of LATE, a commonly occurring disease mimicking Alzheimer's, for which our Center now is conducting the first ever clinical trial, and our bench-to-bedside studies examining the impact of traumatic brain injury on later life cognitive impairment. You will read about the reasons our many research participants volunteer for our studies, and learn about some of our efforts to help in the community.

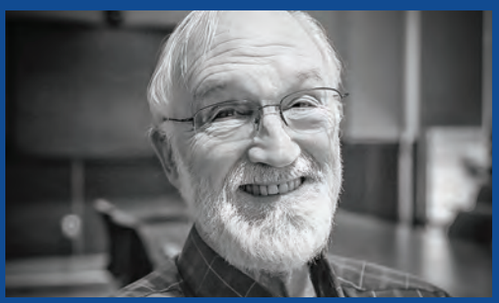
During the past 18 months, Sanders-Brown Center on Aging has been developing a strategic plan to guide our growth over the next ten years. Finalized in 2022, our strategic plan is built on our overarching mission: to enable healthy brain aging for all adults in Kentucky and beyond. In 20 years, our vision is that people will be delaying the start of Alzheimer's disease and related dementias and stopping its progression long before it overtakes them. It is this mission and vision that our center strives for every day.

Words cannot express how incredibly grateful we all are for our research volunteers who continue to give so much of their time, and themselves, to advance our research—without their efforts we would not be able to make the discoveries we do. Within the University of Kentucky, Sanders-Brown is one of the most successful units on campus for federal research funding. We are also appreciative of the many donations we receive annually. As you will learn in the following pages, much of our research success would not be possible without the donations, large and small, received every day. Thanks to our donors, our volunteers, and the tireless work of our faculty, staff and students, we remain a top Alzheimer's disease research center in the nation and the world. A sincere and heartfelt thank you to everyone involved! I welcome your questions and comments and would be delighted to host anyone for a tour of our facilities and an opportunity to tell you more about our work.

Regards,
Linda Van Eldik, PhD
Director, Sanders-Brown Center on Aging

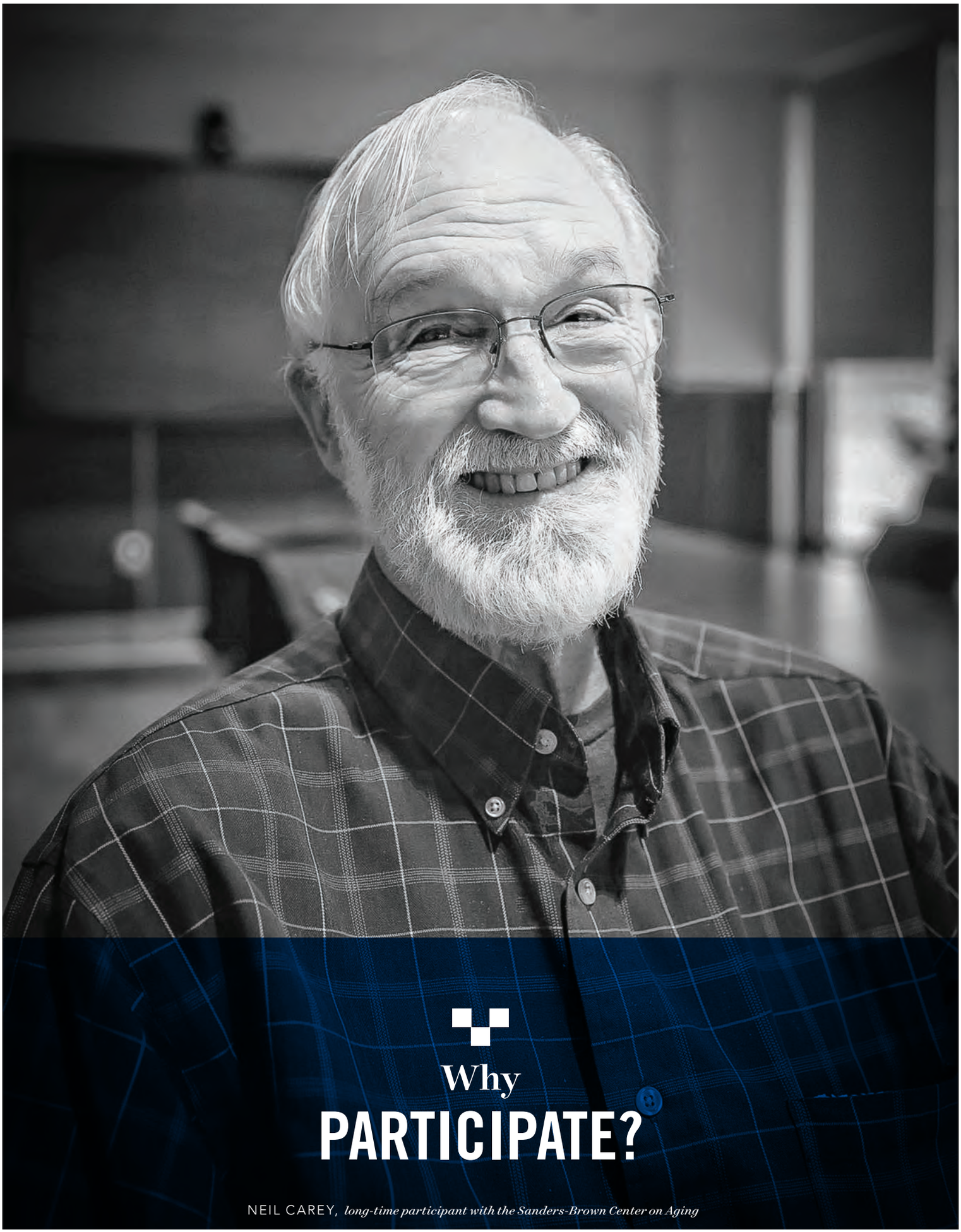
TABLE OF *Contents*

MIND MATTERS | ISSUE 3 | FALL 2022



medicine.uky.edu/centers/sbcoa | UK Sanders-Brown Center on Aging | @UKSBCoA | Sanders-Brown Center on Aging

EDITORS Donna Wilcock and James Haggie | **DIRECTOR** Linda J. Van Eldik | **DESIGN** The Williams McBride Group
PHOTOGRAPHY Arden Barnes, Mark Cornelison, James Haggie, Tim Webb, Melissa Weber | **CONTRIBUTING WRITERS** Rena Baer, Emily Bratcher, James Haggie



Why PARTICIPATE?

NEIL CAREY, *long-time participant with the Sanders-Brown Center on Aging*

Patient STORY

WRITTEN BY JAMES HAGGIE | PHOTOGRAPHY BY JAMES HAGGIE AND UK HEALTHCARE COMMUNICATIONS

"A LITTLE BIT OF ME IS *always working at* SANDERS-BROWN."

—CLINICAL TRIAL PARTICIPANT

Here at the Sanders-Brown Center on Aging, clinical studies are the key to the discovery of novel treatments for Alzheimer's disease and related dementias (ADRD).

At our brand-new clinic at UK HealthCare's Turfland campus, we ask two critical questions on the road to develop a treatment for ADRD: What causes the condition? And does the proposed treatment work?

Clinical research studies fuel the discovery of new treatments and determine whether a treatment impacts the disease, but why, and how, do research partners get involved in the first instance? While there are many factors in deciding to participate in a clinical study, one of the key reasons we encounter from our research volunteers is the desire to be an active participant in their own health care.

> "It is tremendously important for me to be able to understand what is going on during my life's journey, and to be able to make informed decisions regarding my health care using the information that I have from participating in clinical studies," noted Neil Carey, a long-time participant with the Sanders-Brown Center on Aging.

"If you know what you are dealing with, you can strategize and plan a course of action to combat, or at very least, to slow down what is happening," he adds, before mentioning what he stresses is the added benefit of clinical research participation: "What we do and learn in the clinic also benefits everyone else that has the same issues as we do!"

The Sanders-Brown Center on Aging clinic houses over thirty staff and faculty who work together to care for our research participants, ensuring their medical needs are not compromised during participation, and that their memory care is both comprehensive and innovative. Our staff and faculty oversee the safety of all the research our participants are involved in. "Safety and well-being of our volunteers is the number one priority of every person working at the clinic. If there are any doubts about an experimental treatment or procedure, we do not participate in that study," states Dr. Gregory Jicha, the director of the clinic.

> Our ultimate goal is that whenever that first successful treatment for Alzheimer's disease is discovered, our volunteers will be the first in the nation to benefit and have access to it".

For many of our volunteers, they participate in research because they have experienced firsthand the impact Alzheimer's disease and related dementias have on families. For some, they have provided care to their spouse or parent as they progressed through the disease, while for others it is a more distant relative whose disease impact has rippled through the entire family. The desire to actively participate in studies that could lead to the prevention and treatment of dementia for the next generation is echoed through many of our volunteers. Keisha Jones, clinic recruitment coordinator, states "For many volunteers I speak with, their desire to contribute so that nobody else has to go through the pain of watching a loved one decline with dementia is so strong, and they feel empowered by volunteering their time to our cutting-edge research."

A common misconception is that a clinical research study always involves the delivery of an experimental medicine. This is not always the case, and often prevents individuals from volunteering for research. Our clinical research studies are examining a whole host of different

> For many volunteers I speak with, their desire to contribute so that nobody else has to go through the pain of watching a loved one decline with dementia is so strong, and they feel empowered by volunteering their time to our cutting-edge research."

—KEISHA JONES
Clinic Recruitment Coordinator

interventions, sometimes involving medications that have been proven safe, and sometimes observational studies with no intervention at all. Oftentimes, the interventions we are studying are behavioral, like exercise programs or stress reduction, or involve controlling risk factors like blood sugar and blood pressure. We even have interventions that aim to reduce the number of prescribed medications an individual is taking to lower the effect they may be having on the brain's functioning. Our interventions also range from participation by healthy individuals through to individuals already living with a dementia diagnosis. For those with dementia, we have quality of life interventions like art and music therapy, sensory interventions such as aromatherapy, and numerous additional multi-modal approaches. Of course, there are a number of medication studies that we are involved in. Some of these are experimental medicines that have already moved through the critical safety aspects of their testing. Other medications are already approved by the Food and Drug Administration for other conditions, and there may be evidence from our companion laboratory scientists that these particular agents may also benefit dementia, so naturally we look to do a trial in our clinic to investigate further.

Another element that links all of our participants, from the inception of clinical work at the Sanders-Brown Center on Aging to the present day, is that of altruism. Because there is as yet no single blanket treatment, clinical studies continue to rely on voluntary participation to investigate both medicine-based and observational potential treatments, and without those volunteers there would be no progress. However, researchers also acknowledge the role of diversity and inclusion in clinical studies, as not everyone experiences ADRD in the same way—a term called "generalizability." An intervention, whether a medication or a behavioral intervention, that has only been examined in a single demographic, such as Caucasians, may not be generalizable to the more representative population across the community, the country or even the world. As such, it is critical that our research studies be inclusive and representative of the general population, as only this will ensure that an intervention is truly beneficial to everyone. The African American community is at a significantly increased risk of dementia later in life, as are the Hispanic community, yet these populations are traditionally underrepresented in research studies. The Sanders-Brown Center on Aging continues to actively work on lowering this rate of disparity, and to provide programs that benefit all of our communities. ■

GET INVOLVED

Participation in research is the only way we can hope to find cures for diseases such as Alzheimer's disease and promote normal healthy brain aging for all. To discuss how you can participate please call us at (859) 323-5550. Or, complete our online research interest form and we will get back in touch with you soon.

Research STORY

WRITTEN BY EMILY BRATCHER | PHOTOGRAPHY BY MELISSA WEBER & MARK CORNELISON

IS NICORANDIL THE ANSWER?

New Clinical Trial Tests Effectiveness Against LATE

For years, the scientists, researchers and statisticians at the Sanders-Brown Center on Aging have performed groundbreaking research on a neurodegenerative disease called LATE. **Now their research has resulted in a clinical trial for a medication that can potentially prevent the disease.**

Forgetfulness. Memory loss. Confusion. Mental decline. Disorientation. Dementia's effects are many, varied and terrible, but a new clinical trial at the Sanders-Brown Center on Aging is paving the way for the prevention of those symptoms for millions of people affected by a neurodegenerative disease called LATE.

Helping to lead the effort for the Sanders-Brown Center on Aging (SBCoA) at the University of Kentucky is Dr. Peter Nelson, who says "This is what really gets me up in the morning—that we could have a drug to fight LATE and that we could treat it and prevent it."

JOURNEY TO A CLINICAL TRIAL

LATE disease, which stands for Limbic-predominant Age-related TDP-43 Encephalopathy, mimics Alzheimer's in that its symptoms—dementia and amnesia, for example—are similar. The difference between the neurodegenerative diseases comes in the presence of certain misshapen proteins. With Alzheimer's, the tau and the beta-amyloid proteins are misfolded, while the misfolded TDP-43 protein shows up in the brains of people with LATE disease.

"People from around the world had been noticing some degree of evidence of this, so it was a matter of getting everybody together to have a consensus to describe it, to classify it, to be able to diagnose it," says Dr. Peter Nelson, Professor of Pathology at the University of Kentucky and Associate Director of Sanders-Brown Center on Aging. The work resulted in a study published in 2019 in *BRAIN: Journal of Neurology.*

In addition to leading up the efforts to codify the disease, Dr. Nelson has also spearheaded the work in determining the prevalence of the disease. Gathering 13 different cohorts from five different countries and three different continents, he discovered that LATE is widespread among people in their late-80s.

> "The bottom line is that about **40% of people in advanced old age have LATE pathology**," Nelson says. "It's very, very common. This leads to a very important follow-up point: **a lot of what we previously were calling Alzheimer's disease, was actually LATE."**

Since SBCoA is focused on preventing or curing diseases, the next step was determining the genetic risk factors, which affords a foothold for finding a therapeutic solution.

In 2014, Nelson, in collaboration with statistical geneticist Dr. David Fardo (also a professor of biostatistics,) performed Kentucky's first Genome-Wide Association Study (GWAS) for LATE.

In performing the GWAS, Fardo explained that they were interested in discerning the potential roles of DNA variants—and how could variation in a particular DNA variant affect downstream disease processes?

"If that variant is associated with a protein that is a drug target, then you can potentially interrupt the pathway from variant to disease and reduce the downstream proteinopathy," Fardo says.

What they found—and what ultimately led to the clinical trial—came as a welcome surprise: There was an association between genetic variation in the ABCC9 gene and LATE.

"It was a 'druggable' target," Nelson says. "The gene makes a protein and the protein can be affected by medicines that are commonly taken."

Over the next several years, Dr. Gregory Jicha, a UK professor of neurology and associate director of SBCoA, worked with Nelson on identifying a drug called Nicorandil that could possibly prevent LATE.

THE WORLD'S *only* LATE CLINICAL TRIAL RUNNING PRESENTLY,
and it's all based at the University of Kentucky.

LATE CLINICAL TRIAL *at a glance*

64
PARTICIPANTS

75
YEARS OR OLDER

6
MONTH SUPPLY OF MEDICATION AT A TIME

VISITS EVERY
6
MONTHS

TAKE MEDICATION FOR
2
YEARS

5
YEAR CLINICAL TRIAL

THE START OF A NEW CLINICAL TRIAL

After receiving funding from the National Institute on Aging (an Institute of the NIH), SBCoA set to work in establishing the trial.

> We have the best place in the world to do clinical trials right here at the University of Kentucky. Dr. Jicha and his team are amazing," Nelson says, adding that now that the pandemic is waning, the time is right for finding a cure for the awful disease.

Currently in the recruiting phase, the LATE clinical trial can accommodate 64 participants who will go through a screening process that includes bloodwork, memory testing, an exam with a clinician, an MRI and a lumbar puncture to determine whether they have risk for LATE. Some of the people may be at risk for other conditions, and there are also available clinical trial options that can be discussed with the clinicians at SBCoA.

To be a good fit for the LATE trial, participants are ideally 75 years or older, and they need to have a certain level of cognitive function. Potential participants who are taking some drugs or agents that would either muddy the results or cause harmful interactions would not be a good fit. Those who've been diagnosed with Parkinson's or who have experienced strokes would not be suitable for the trial. But if they're eligible for the trial, the participants will be

randomly prescribed a course of placebo or Nicorandil. They'll also designate a "study partner," usually a family member, who will come alongside them and assist with the trial.

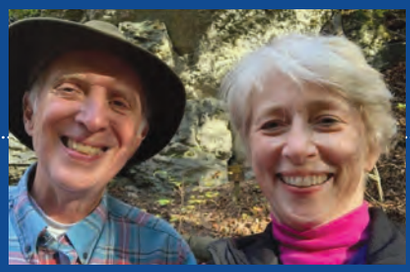
"We give them a six-month supply of medication to take home along with instructions on doses and how to take the medication," says Danica Coy, Clinical Research Coordinator for LATE. "They come back four weeks after starting the medication for more blood work and vitals to confirm that they are not having any adverse effects from the study medication. After that, they will come in for a visit every six months for two years where they will undergo the same procedures completed at screening to check for any changes in labs or memory testing scores."

Patients will also undergo two additional MRIs and another lumbar puncture at the end of the trial to identify whether the medication has decreased the risk for further memory decline. Along the way, they'll also be monitored for any side effects, and they're asked to inform SBCoA about any changes in their health that they might be experiencing.

Although participants will take the medication over a two-year period, the clinical trial itself will run across five years.

The LATE research program and clinical trial is unique in that it's the world's only LATE clinical trial running presently, and it's all based at the University of Kentucky.

> It's super humbling, and it's a testament to the incredible research volunteers, the amazing people at Sanders-Brown, the diversity of expertise, and the willingness and ability for that different expertise to meld together to make trans-disciplinary science happen," Fardo says. ■



A PARTICIPANT'S *Perspective*

Several years ago, Lu-Ann Farrar noticed that her husband Ned of nearly 40 years was experiencing worsening memory. In February of 2018, he underwent a brain scan as part of a longitudinal study at the University of Kentucky's Sanders-Brown Center on Aging, and what they found was interesting. Noticeably lacking were the telltale plaques and tangles characteristic of Alzheimer's.

In a meeting with Dr. Jicha, Lu-Ann remembers asking, "Is this good news or bad because clearly he has dementia?"

Dr. Jicha replied: "Anytime someone tells you, your brain is not full of beta amyloid, that's a good thing."

Instead, he said that Ned looks like he could have LATE disease. During that meeting, he told Lu-Ann about a clinical trial in the works for a drug used abroad to treat heart disease in older people that they thought could have some efficacy in preventing LATE disease.

Although the COVID pandemic delayed the trial, Ned was first in line when the trial opened this past spring.

"It's been very easy," Lu-Ann says. "I just put his pills in his pillbox, and he takes them."

In addition to that, Lu-Ann coordinates his appointments and communicates with his health care team at Sanders-Brown.

When asked about why they were interested in the clinical trial, Lu-Ann says "hope." The hope is that the drug would somehow stop or slow the effects of the disease.

"As I say, [dementia] is death by a thousand cuts. I'm not the first person to go through this, not the first person to see it, but it's a slow drip-drip of loss," she said. "For a disease like this, you literally don't have anything to lose. You might as well try it, and see what happens."

With profound gratitude we fondly remember all of our cherished partners in research.

Donor STORY

WRITTEN FROM AN INTERVIEW BY UK PHILANTHROPY | PHOTOGRAPHY BY TIM WEBB

VIRGINIA BELL

Bringing the Dream Forward

To say Virginia Bell has lived a full life is a vast understatement. Besides being a newly minted centenarian, she has traveled the world, written several books, raised five children and formed friendships with countless people with dementia.

This idea of friendship is what Virginia wants you to hear in any conversation you have with her. Since first coming to the Sanders-Brown Center on Aging in 1980 as a social work practicum student, she has prioritized building relationships with patients—a seemingly simple idea that revolutionized care for people with dementia.

One of her first assignments at Sanders-Brown was to sit with dementia patients during a family support group. "The people with dementia were terribly upset because they were separated from their family in a new building, and they didn't even know who I was, and I didn't know anything about their life story. I said, 'We have to change that.'"

> “I brought my dream forward, but that wasn’t enough. I’m counting on you all to do your part.”
>
> —VIRGINIA BELL

Throughout the next 40 years, that’s exactly what she’s done. She says her practicum committee was skeptical when she first suggested using friendship as a mode of care, but eventually she persuaded them to let her try it one day per week. “We opened in 1984, and in 38 years we’ve never had anyone yet that we’ve not been able to keep. People can come in angry, and that’s common, but if you lift the dementia and look underneath, you find a unique person. Creating a friendship with that person helps them feel oriented and can dissolve those behavior problems.”

Her so-called “Best Friends” approach has been replicated on a national and international scale, creating communities that care for dementia patients as people first, disease second. “It’s not rocket science,” she says, “it’s kindness.”

Though Bell has spoken in over 100 different places about the Best Friends approach, she has always maintained a deep connection with Sanders-Brown. When asked why she keeps coming back to Sanders-Brown, both as a donor and a volunteer, she initially talks about it being the place where she had the first core idea. But she then takes an unexpected turn, into talking about her childhood, her community and her life on a farm—and after describing a quality about someone she says every time: “I brought that forward.”

Virginia Bell has brought her entire 100 years’ experience, and her entire life’s community, forward into her work with Sanders-Brown and dementia care. “I brought my dream forward, but that wasn’t enough,” she says. “I’m counting on you all to do your part.”

Philanthropy IMPACT

> “Thanks to philanthropy, we are thrilled that we can provide on-site infusions for some of our cherished research participants. Generous donations have allowed us to offer more studies, which means there are more treatment options through our clinic as we work to end the debilitating effects of dementia.”
>
> —ALEXANDRA HUNTER
> *Clinical Trial Coordinator*

> “It is difficult to express how valuable philanthropy is to our research successes, and to our progress improving the lives of our aging population. The Wilcock laboratory has been the beneficiary of philanthropy dollars that were used to purchase technologically advanced equipment, allowing us to analyze patient blood samples drawn at clinic visits, and predict whether they might have Alzheimer’s disease changes in their brain without them having any symptoms. As a result, we now have several research grants that are allowing us to pursue this research with a goal to develop personalized treatment approaches in the future.”
>
> —DONNA M. WILCOCK, PhD
> *Assistant Dean of Biomedicine*
> *Associate Director, Sanders-Brown Center on Aging*

Philanthropy helped build the first facilities for Sanders-Brown more than 40 years ago, and philanthropy is essential today to advance our mission of finding a cure for Alzheimer’s and related diseases. Our new memory clinic, opened in 2022, provides a seamless, less stressful experience for patients and their families. With a total philanthropic goal of $10 million over the next five years, we will expand our facilities, support clinical research, enhance educational programming, and establish a training fellowship for improved patient care. We have a bold vision for the future, and with your generous philanthropic support, we’ll be ready to meet the needs of our aging community for generations to come.

For more information or to support Sanders-Brown Center on Aging, scan the QR code, visit **https://bit.ly/SBCoAFund**, email **gratitude@uky.edu** or call **859-323-6306**.

the impact of ONE PERSON

191
BIO-SPECIMENS

USED BY
43
RESEARCHERS

IN
76
STUDIES

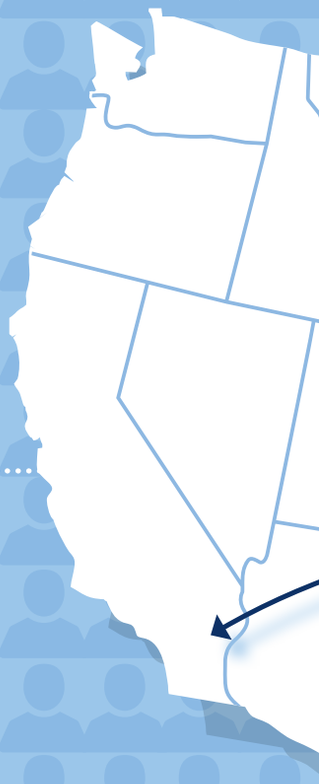
x787
PARTICIPANTS

what TYPES OF BIO-SPECIMENS?

- Frozen tissue
- Fixed tissue
- Bloods
- CSF clinical
- CSF postmortem
- Slides with fixed tissue

where ARE THE RESEARCHERS?

- **13** Sanders-Brown
- **10** University of Kentucky
- **20** Outside the University of Kentucky



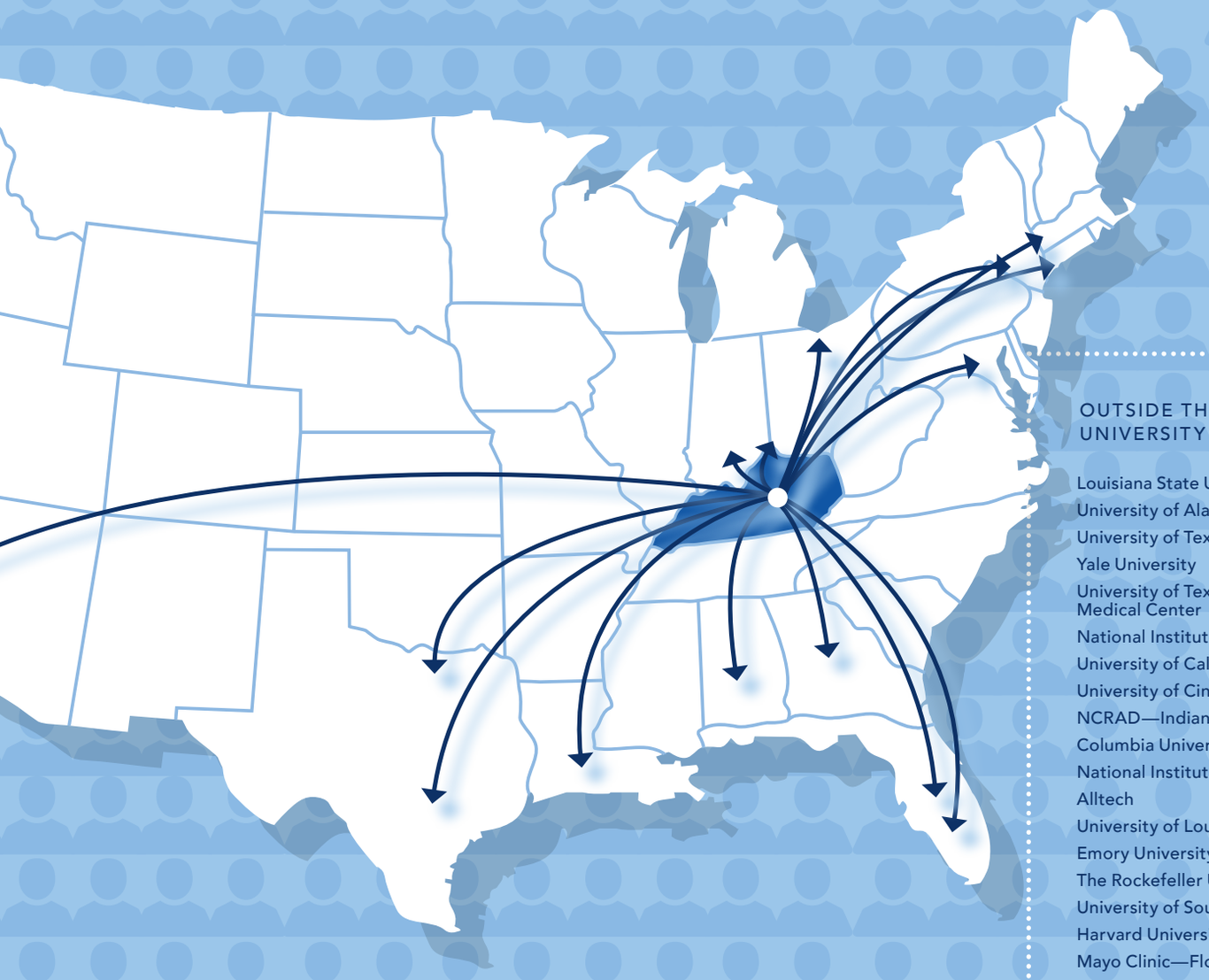
what TYPES OF STUDIES?

- Alzheimer's blood biomarkers
- LATE studies
- Tau pathology in Alzheimer's disease
- Genetic risk factors of dementia
- Diabetes and dementia relationship

What does it take to change the world? The researchers at the Sanders-Brown Center on Aging can tell you: one person.

Each of the 787 participants in our clinical research studies knows their reasons for taking part. Maybe they want to get ahead of unknown health issues. Maybe they feel like they're serving their communities. Maybe it's personal for them. What they may not know is how their individual contributions can exponentially benefit researchers' efforts to guarantee healthy brain aging to populations across the globe.

One person: 191 opportunities. That's 191 opportunities to find new treatments, to discover new drugs, to uncover new diseases. **191 opportunities to find a solution.**



OUTSIDE THE UNIVERSITY OF KENTUCKY

- Louisiana State University
- University of Alabama
- University of Texas
- Yale University
- University of Texas Southwestern Medical Center
- National Institute on Aging
- University of California, San Diego
- University of Cincinnati
- NCRAD—Indiana University
- Columbia University
- National Institute of Health
- Alltech
- University of Louisville
- Emory University
- The Rockefeller University
- University of South Florida
- Harvard University
- Mayo Clinic—Florida

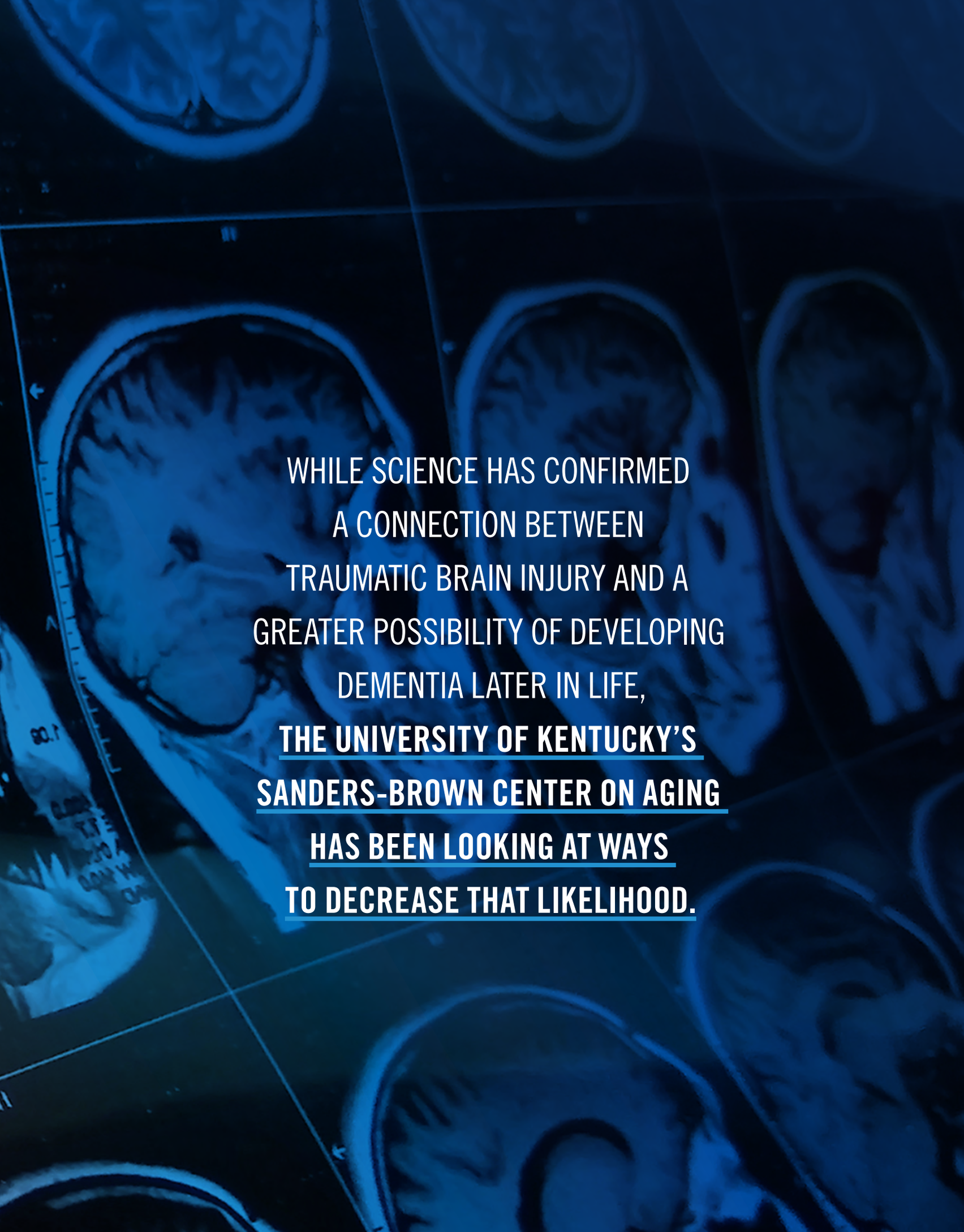
This graphic has been designed using resources from Flaticon.com

Research STORY

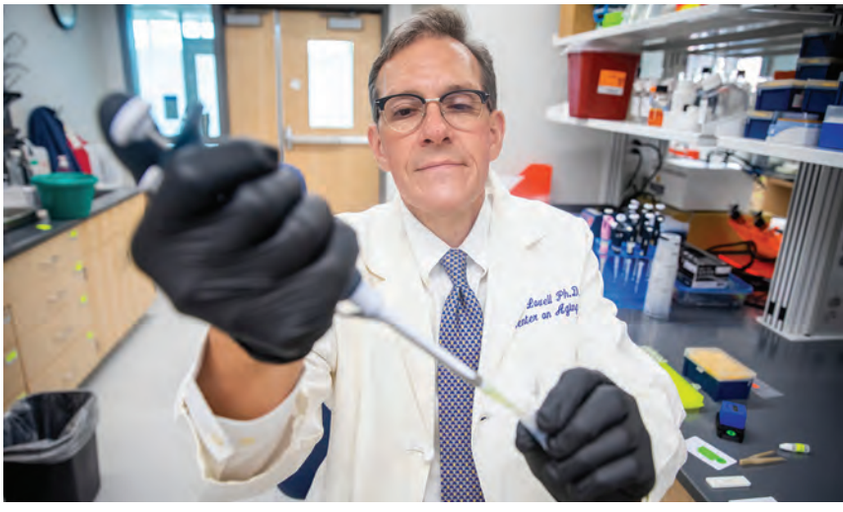
WRITTEN BY RENA BAER | PHOTOGRAPHY BY MARK CORNELISON

"EVERYONE IS AT RISK, ALL THE TIME."

Sanders-Brown researchers study, diagnose and treat Traumatic Brain Injury



WHILE SCIENCE HAS CONFIRMED
A CONNECTION BETWEEN
TRAUMATIC BRAIN INJURY AND A
GREATER POSSIBILITY OF DEVELOPING
DEMENTIA LATER IN LIFE,
THE UNIVERSITY OF KENTUCKY'S
SANDERS-BROWN CENTER ON AGING
HAS BEEN LOOKING AT WAYS
TO DECREASE THAT LIKELIHOOD.



"We are working on a lot of diseases and injuries that are high risk factors for later dementia, and traumatic brain injury is just one example, but it's a huge risk factor," says Dr. Linda Van Eldik, director of Sanders-Brown.

A team of researchers has been exploring biomarkers, such as inflammation and mitochondria, that react after a mild traumatic head injury (TBI), such as a concussion, which accounts for more than 80% of head injuries. They are also discovering novel and quick ways to test for those markers and are exploring possible therapeutics to try and mitigate the damage "upstream." In addition, they are studying the cellular pathology of TBI in older subjects compared to younger subjects to see if there's a way to restore the brain's ability to regulate itself (homeostasis).

Between 1.7 and 3.8 million Americans suffer TBI each year. TBI occurs when there is a sudden external force that damages the brain and is one of the most common causes of disability (and death) in the United States. When most people hear about TBI, they think of football players and other athletes, but sports- and recreational-related TBI only account for 10% of cases. More people sustain TBI from falls, auto accidents and violence (including domestic violence and being shaken).

"Everyone is at risk all the time for a TBI," says Dr. Adam Bachstetter, an associate professor in UK's College of Medicine's Spinal Cord and Brain Injury Research Center, which is working in tandem with Sanders-Brown.

> "You could be walking down the hall and the floor has just been mopped and you slip and hit your head. You could be in a car accident. So it's important to know whether that injury might have a lasting effect on your brain."

Dr. Mark Lovell, professor and chair of UK's Department of Chemistry, and his team have developed a lateral flow device, much like a home pregnancy test or home COVID test. The device detects a novel marker of neuronal injury from a drop of blood from a fingerstick. Because it's a quick test and doesn't require extensive instrumentation for detection, it can be used at "the point of care," says Dr. Lovell.

DID YOU KNOW?

BETWEEN
1.7 & 3.8 MILLION
Americans suffer TBI each year.

ADULTS AGES
65 YEARS OR OLDER
had the highest rates of TBI-related hospitalization with a rate higher than all other ages combined.

"In our recent studies we worked with UK sports physicians [Drs. Kyle Smoot , Robert Hosey and Kim Kaiser] and athletic trainers to evaluate the marker in male and female athletes at baseline and following sports-related concussion [SRC]. We were able to demonstrate that the marker does not change due to normal physical activity but increases substantially following a concussion."

Dr. Lovell says they are working on adding additional test lines to the device to determine the severity of the injury. The current standard of care relies on the injured person to self-assess his or her symptom severity, memory tests and an assessment of balance, along with other criteria, and is carried out by a team physician or athletic trainer. It is more subjective than the objective assessment provided by the device.

"In addition to the potential use for sideline point-of-care assessment of SRC there is also potential for use of the device in the emergency room," he continues. "Current guidelines from the American Academy of Pediatrics recommend limited use of CT scans for children unless there is a clear indication of need. It's possible that the lateral flow device could be used as a pre-screen by the ER staff to argue for brain imaging."

Dr. Van Eldik has targeted similar biomarkers to develop a therapeutic drug candidate compound that targets that injury-induced brain inflammation. Using mice as TBI model systems, she and her team administered the compound for only a few days while brain inflammation was occurring after injury. Thirty to 60 days later the positive changes in cognition were still seen, she notes.

"Even if the drug is no longer there, because you've blocked something upstream that causes downstream damage to cognitive function, the downstream cognitive impairment doesn't happen," says Dr. Van Eldik. "In TBI, a person could have a brain injury and take our drug when they get to the hospital and for the next few days while they are still having an inflammatory response. And when they stop the drug, it would still have long-lasting benefits. That's the goal."

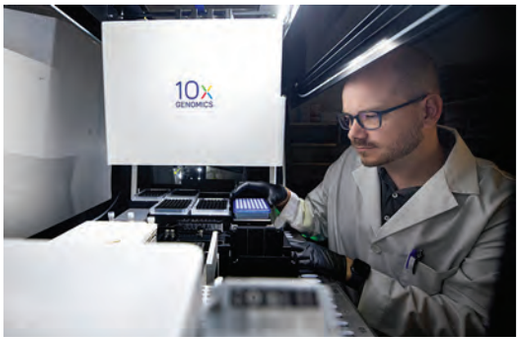
One huge advantage of this compound is it singles out harmful inflammation. "It only blocks the overproduction of these inflammatory molecules caused by injury or disease," she says. When unregulated, this overproduction mechanism can cause the brain to get "out of whack," and scientists are discovering its role in many different diseases such as Alzheimer's and Parkinson's, not only brain injuries. And even as healthy individuals age, that inflammation goes up to the high end of normal. "Even the slightly elevated inflammation responses seen in normal aging can have effects on other cells and other components of the brain because cells are interacting."

That difference is the reason that Dr. Josh Morganti, assistant professor in UK's Department of Neuroscience, has been studying how the brains of older animal subjects respond when TBI occurs. Most research in TBI, he says, has been modeled in young animals that map to ages between early and middle adulthood, which are actually the years when the fewest TBI occur.

> "We've published many times that the older brain's response to trauma is highly exaggerated relative to how a young brain would work," he says.

He notes that rather than return to their pre-injury state as they can in younger subjects, the immune cells, or microglia, of older subjects maintain a heightened response that can persist years after an injury. "We're interested in how we can get them back to their pre-injury [self-regulating] status."

This is important because TBI at an older age carries an increased risk for developing dementia and in a shorter period. "We are trying to understand what's driving that," says Dr. Morganti. "We only want to go after the cells that are being problematic and try to identify something unique about them that is 'druggable.'"



Dr. Bachstetter says while TBI can happen to anyone at any time, these injuries are most prevalent in older adults, who are more prone to falling, and young children learning to walk and explore.

He says his lab is studying mild TBI and how it can accelerate the risk for developing dementia later in life and also how suffering a TBI affects the rate of decline in subjects that already have Alzheimer's or dementia-related pathology.

"We are in the early stages at this point, looking at how animals' brains respond to injury at different ages and watching, as they age, whether it changes their ability to perform tasks," he says, adding that they are also examining inflammatory processes and mitochondrial function. "We're looking at the ability of their brain to make and use energy after injury."

Dr. Bachstetter has been working with Dr. Christopher Norris, a professor in UK's Department of Pharmacology & Nutritional Sciences, studying how a particular chemical (a cytokine) that's released during neuroinflammation affects the brain after a mild TBI.

Most of Dr. Norris' research is in Alzheimer's disease, but he says there are a lot of parallels between the two. "There is a lot of brain inflammation in traumatic brain injuries that you see in Alzheimer's disease, and certain neural circuits are hyper excitable in both.

"There are these common mechanisms between the two, but the environmental risk factors for Alzheimer's are very elusive. But what we do know is if you have a brain injury, especially a repetitive brain injury, your risk of getting Alzheimer's goes up quite a bit.

"It's like if you have a repetitive knee injury and later develop arthritis in that knee," he says.

The hope behind their current research, he says, is to reduce cognitive loss and improve the brain's ability to recover after a TBI and see if it reduces the risk of later neurodegenerative disease.

> "And the more we can learn about TBI, the more we can learn about Alzheimer's," he says.

Dr. Pete Nelson, UK College of Medicine's director of Neuropathology, has noted in autopsies that some brain changes seem to happen in both dementia and TBI. "We are trying to tease them out because maybe having a therapeutic strategy, like Dr. Van Eldik is doing with TBI, could have applications for dementia research."

And as time goes on, and with the greater recognition of TBI's connection to dementia, more information will become available to aid in catching and treating TBIs "upstream," cutting down on the likelihood of developing related dementia later.

"We are leading the world in this type of research, and I don't say that lightly," says Dr. Nelson. "It's the reason why I came here."

Meanwhile, Dr. Morganti has advice for everyone: helmets, helmets, helmets, on bikes, scooters, motorcycles or during any activity where the likelihood of falling increases.

"There's just no way to prognosticate a TBI," he says. "It can just come down to a weird crack in the sidewalk, and a kid hitting it on a skateboard and falling funny. It's not going to prevent a TBI necessarily, but it'll mitigate its severity for sure." ■

TRAUMATIC BRAIN INJURY
DID YOU KNOW?

IN 2019,
15,000
PEOPLE
visited Kentucky hospitals with a TBI-related injury.

11,666
WERE TREATED & RELEASED FROM AN ED

3,252
WERE HOSPITALIZED

2,216
TBIs occurred among children ages
0 *to* **14**
YEARS

ED VISITS
accounted for
more than
90%
OF THE TBIs IN THIS AGE GROUP.

41
STATE RESIDENTS PER DAY
being treated for TBI in Kentucky hospitals (ED and hospitalization)

2
TBI-RELATED DEATHS PER DAY

FALLS
WERE THE LEADING CAUSE OF TBI for both ED visits as well as hospitalizations. **ED rates were highest for children ages 0 to 4 years and for adults 65 years or older.**

FALLS RESULTED IN THE
GREATEST NUMBER OF TBI-RELATED HOSPITALIZATIONS

2.4X *more* THAN
MOTOR VEHICLE TRAFFIC CRASHES.

WRITTEN BY JAMES HAGGIE

MEMORY SUNDAYS

The Outreach, Recruitment and Engagement Core (ORE) represents the connection from the Sanders-Brown Center on Aging to the community. From maintaining a social media presence to sharing updates on current clinical studies at the center, through to the distribution of educational materials at community events, the ORE Core is a powerful source of information, education and support.

One specific area of outreach for the ORE Core is into the historically under-resourced faith community, the flagship event of which is "Memory Sunday", designated nationally as the second Sunday in June. The specific aim of Memory Sunday is to use fellowship to raise awareness on Alzheimer's disease and related dementias, and the disproportionate impact they have on African American communities, the incidence rate for whom is two to three times higher than for Caucasians.

The genesis of Memory Sunday resides in the ORE Core here at the Sanders-Brown Center on Aging. Now led by Derrick Hord and Markeda Yarbrough, who both passionately believe that resource sharing is best augmented by a physical presence in the community, the aim is to serve families who may otherwise have minimal opportunity for support in a culturally appropriate manner. Utilizing the framework established in The Book of Alzheimer's for African American Churches, also developed by the ORE Core, Hord and Yarbrough continue to facilitate Memory Sunday events during morning worship, dedicated both to those who are affected by memory disorders and their caregivers.

Since the first occurrence, more than 50 churches have incorporated Memory Sunday events during the month of June, and momentum continues to grow. During each event, support and resources are offered to the faith community, including information on how to access services at Sanders-Brown, the importance of diversity and inclusion in clinical studies to develop useful treatments to serve our communities, and recognition in the form of commemorative memorabilia to celebrate unity. Every day, the ORE Core offers gratitude to participants of both past and present Memory Sunday events. The event has proven to draw national attention, and is now supported nationally by The Balm In Gilead, Inc., a non-profit organization that develops educational and training programs specifically designed to establish sustainable, integrated public health and faith principles to improve outcomes for individuals living in urban, rural and remote communities. ■

For further information, or to contact the ORE Core, please call Markeda Yarbrough at (859) 218-3867.

Student PROFILE

WRITTEN BY & PHOTOGRAPHY BY JAMES HAGGIE

PATRICIA DOYLE

Patricia Doyle's interest in science grew from experience as a musician and an interest to understand how music affects the brain. She grew up with grandmothers suffering from Alzheimer's disease (AD) and amyotrophic lateral sclerosis (ALS), who she noticed responded positively to music. This interest in neuroscience grew into a passion and a drive to understand how and why neurodegeneration progresses.

Doyle entered the University of Kentucky Integrated Biomedical Sciences (IBS) PhD program with a record of research excellence that includes extensive volunteering in research environments, two summer research programs at West Virginia University and the University of North Dakota, as well as a post-baccalaureate internship at The Jackson Laboratory led by Drs. Kristen O'Connell and Catherine Kaczorowski.

She began IBS rotations at the University of Kentucky in the Fall of 2020 with the intention of pursuing lab rotations in the world-renowned Sanders-Brown Center on Aging. The availability of prestigious fellowships, numerous novel research seminars, and the plethora of clinical samples of AD from research participants made Sanders-Brown a perfect fit for Doyle to achieve her goals.

As a result of her rotations, Doyle found a home in the lab of Dr. Mark Ebbert, where she now explores themes in neurodegenerative diseases, Alzheimer's disease and related dementias (ADRD), and genomic approaches. The Ebbert lab ties together many aspects of research that Doyle finds especially interesting while also providing a collaborative environment in which her research goals are supported and encouraged.

Spending her graduate career at Sanders-Brown will bring a new perspective to Doyle's past research and prepare her for competitive research professorships after completion of postdoctoral work and beyond, which includes a strong desire to mentor the next generation of neuroscientists.

Whatever the future holds, Doyle is keen to highlight what is important to her about Sanders-Brown. "I absolutely love this community of researchers! Colleagues and mentors are willing to lend out study compounds and reagents, to share scientific instruments, and to pass along skills when they can. They are so supportive! As an early-career researcher this is a great environment to learn in, and I'm very proud to be a part of that." Doyle is also an advocate for accessibility, diversity, and equity in science and scientific research, and strives to foster environments where scientists from differing disciplines and with varied backgrounds can come together and succeed. ■

ALZHEIMER'S *in* KENTUCKY

2022

Alzheimer's disease is a growing public health crisis in Kentucky. Without an effective treatment or cure, the impact of Alzheimer's will continue to rise, and the numbers in Kentucky are escalating.

NUMBER OF PEOPLE
AGED 65 AND OLDER
living with Alzheimer's in Kentucky

estimated
14.7% CHANGE

2020 **75,000**
2025 **86,000**

6th LEADING CAUSE OF DEATH

1,684
DEATHS FROM ALZHEIMER'S DISEASE (2019)

150,000 *family caregivers*
bear the burden of the disease in Kentucky

69.6% of caregivers have chronic health conditions

27.1% of caregivers with depression

COUNTIES WITH THE
HIGHEST ADRD PREVALENCE
AMONG BLACKS IN THE NATION

#2 FRANKLIN (20.4%) COUNTY, KY
in the nation

#16 MERCER (14.5%) COUNTY, KY
in the nation

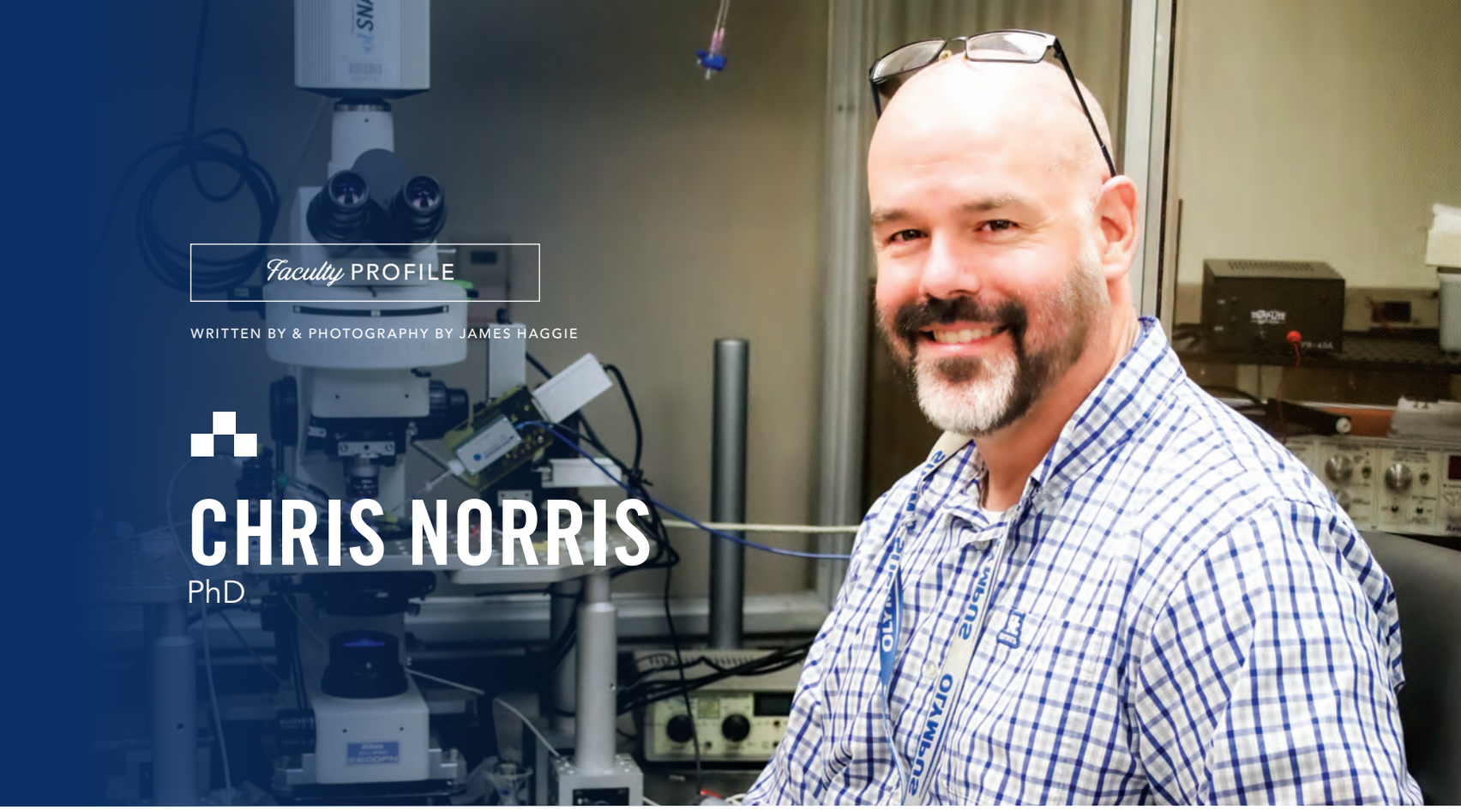
$3.86 BILLION TOTAL VALUE OF UNPAID CARE

WORKFORCE

39
OF GERIATRICIANS *in Kentucky*

430.8%
increase needed to meet the demand in 2050

Alzheimer's Association Facts and Figures 2022



Faculty PROFILE

WRITTEN BY & PHOTOGRAPHY BY JAMES HAGGIE

CHRIS NORRIS

PhD

Chris Norris began his undergraduate studies pursuing a degree in computer science, but after taking a class on psychology he found himself extremely interested in learning not how computers function, but in how people do. "I became very interested in how people learn and remember things, and how the brain works," he states. His curiosity was spurred on by an enlightening and inspiring instructor who he remembers and emulates to this day. Norris' desire to learn more about the brain quickly led to research opportunities in infant cognition, and designing experiments piqued an interest in understanding how cognition is affected when something goes wrong. "The research came naturally, and quickly became about the brain's involvement in learning and memory."

The Sanders-Brown Center on Aging has been home to Norris since 2004, and he credits the uniquely collaborative environment, coupled with the efforts and commitment of the research volunteers and participants, for his success. "As you get older, you start to see friends, you start to see loved ones succumb to dementia, and it becomes personal." After losing his mother to vascular dementia in 2021, Norris finds himself increasingly invested in working toward a successful treatment fueled by personal experience as well as natural academic curiosity. "It's about making a difference in people's lives, and what we are doing with the data we gather from research is incredibly important. Don't be afraid to go where the data is taking you."

Norris now focuses his attention on astrocytes: star-shaped cells in the nervous system. Astrocytes make up a third of the cells in the brain—but for many years they've been underappreciated. These cells have significant roles in neuroinflammation, the regulation of blood flow, the maintenance of synaptic connections, and the regulation of metabolism. Thanks to philanthropic funds, Norris now has a state-of-the-art, laser driven multiphoton microscope in his lab and shares access with multiple collaborators across the Sanders-Brown Center. Multiphoton microscopy allows imaging of the living brain to visualize cellular and subcellular events, previously impossible prior to its development.

> "It has opened a door; now we can ask questions we didn't know we needed answers to because we have the technology to look," says Norris.

When asked where his research will lead, Norris immediately answers with the same passion and enthusiasm he got from his psychology teacher: "Strategies for targeting astrocyte reactivity, and to leave the world a little better than it was when I got here!" ■

STRATEGIC *plan*

The Sanders-Brown Strategic Plan recognizes our strengths, our history and our potential. It identifies areas where we must continue to stand out and areas where we have clear need for improvements. The strategic plan sets ambitious priorities and expectations for our Center to achieve the 20-year vision we have laid out.

1
CAPACITY TRANSFORMATION

2
COLLABORATIVE CULTURE

3
REPUTATION GROWTH

10-year vision

We have attained levels of human, financial and physical capital few of our national peers can match.

CAPACITY TRANSFORMATION

INCREASE CAPACITY *to do* MORE RESEARCH

INCREASE CAPACITY *to* TREAT MORE PEOPLE

COLLABORATIVE CULTURE

10-year vision

Our exceptional contributions to the science and promotion of healthy brain aging are a direct result of collaboration, integration and interdependence.

COLLABORATE
WITH OTHER REGIONAL
ALZHEIMER'S CENTERS

WORK WITH
LOCAL & STATE GOVERNMENT

SYNERGIZE
AND CONTINUE TO
BUILD RELATIONSHIPS
WITH OTHER UK ENTITIES

College of Pharmacy | College of Public Health
College of Engineering | College of Arts and Sciences
College of Health Sciences | Center for Health Equity
Transformation | Saha Cardiovascular Research Center

COMMUNITY
outreach

Sanders-Brown Center on Aging is better known on the National and International level than we are locally. As a Center, we need to be a resource for the local and regional communities for memory care and support. To achieve this, we will enhance our partnerships with local agencies, provide community education programs at the new Sanders-Brown clinic, and provide critical resources to the community including dementia patients, caregivers and all those looking to maintain a healthy brain as they age.

10-year vision

Our regional and national prominence is a magnet for continuous interest and support from institutions, philanthropists, scientists and research participants.

BE PERCEIVED
locally and nationally as
THE LEADING DEMENTIA RESEARCH CENTER

PROMOTE & PROVIDE
SERVICES *to* LOCAL COMMUNITY

REPUTATION GROWTH

Sanders-Brown
Center on Aging

University of Kentucky
789 S. Limestone, Todd 5th floor
Lexington, KY 40536

Nonprofit Org
US Postage
PAID
Lexington KY
Permit 51

“We have the best place in the world to do clinical trials right here at the University of Kentucky. Dr. Jicha and his team are amazing. Now that the pandemic is waning, the time is right for finding a cure for the awful disease.”

—DR. PETER NELSON

Mind Matters is an annual publication from the University of Kentucky Sanders-Brown Center on Aging.